Synthesis of trans-4-methyl-4-hydroxy-2-pentenoic acid

An acid (C₈H₁₀O₃) has recently been isolated in pure state from the essential oil of Bunium cymylriicum (166) by fractional distillation. This is the first report of the occurrence of this acid from a plant source though the acid had already been identified as one of the autoxidation products of bisabolangelone by Novotny et al (167). NMR spectrum of this compound corroborated its structure as (LXXX).

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{H}^{(3)} \\
\text{C} & \quad \text{C} \equiv \text{C} \quad \text{COOH} \\
\text{H}_3\text{C} & \quad \text{OH} \quad \text{H}^{(2)}
\end{align*}
\]

(LXXX)

The trans configuration for H(2), H(3) is also suggested due to the fact that cis acid has been known in the form of its lactone only. This is also supported by I.R. spectrum which gives characteristic bands at 1640, 1620, 930 cm\(^{-1}\) (trans disubstituted double bond) (168). This structure is also supported by its mass spectrum which gives a molecular ion peak (M\(^{+}\)) at m/e 130.

The present dissertation describes a straightforward synthesis of this acid. The approach utilizes the use of Wittig (169) and Grignard reactions followed by
hydrolysis as depicted in the annexed scheme.

\[
\begin{align*}
\text{CH}_3\text{C} & \text{CH}_2\text{Br} \rightarrow \text{CH}_3\text{C} \text{CH=CHCO}_2\text{C}_2\text{H}_5 & (\text{LXXXI}) \quad (\text{LXXXII}) \\
\text{C} & \text{CH=CHCO}_2\text{C}_2\text{H}_5 \rightarrow \text{C} \text{CH=CHCOOH} \\
\text{LXXXIII} & \quad \text{LXXX}
\end{align*}
\]

The bromoacetone (LXXXI) on treatment with carboethoxymethylene triphenylphosphorane in dry benzene (169) in the presence of ethylbromoacetate furnished ethyl 4-keto-trans-2-pentenoate (LXXXII) in 75% yield. The compound (LXXXII) showed characteristic infrared bands at 1720, 1640 cm\(^{-1}\) (unsaturated ester), 1700 cm\(^{-1}\) (keto group), 985 cm\(^{-1}\) (trans double bond). The ketoester (LXXXII) was subjected to Grignard reaction with methyl magnesium iodide in dry ether when ethyl 4-methyl-4-hydroxy-trans-2-pentenoate (LXXXIII) was obtained in 63% yield. I.R. spectrum showed characteristic peaks at 3450, 1040 cm\(^{-1}\) (hydroxy), 1720, 1640 cm\(^{-1}\) (unsaturated ester), 980 cm\(^{-1}\) (trans double bond). The unsaturated ester (LXXXIII) was finally hydrolysed with methanolic sodium hydroxide to obtain trans-4-methyl-4-hydroxy-2-pentenoic acid (LXXX) in 73% yield. The acid was found to give a positive test
for unsaturation (bromine water). The purity of the compound is further checked by t.l.c. (single spot).

I.R. spectrum of the synthetic compound showed characteristic bands at 3245 (tertiary bonded -OH), 2970-2400, 1700, 1670 cm⁻¹ (diffuse for -C-C-COCH), 1410, 1370 cm⁻¹ (\( \text{CH}_3 \)\( \text{C} \)), and 1640, 980 cm⁻¹ (trans disubstituted alkene), identical to those reported in literature (166).

The formulation (LXXX) of the acid was further confirmed by its NMR spectrum which showed characteristic signals at 6 1.39 (s, 6\( \text{H}_2 \)), 6.0 and 7.1 (each doublet, \( J = 16\text{Hz} \), \(( - \text{C} = \text{C} - )\)). This data is consistent with the values reported in the literature (166).